TABLE 25-continued

CYP3A4 Activity in Cryopreserved Human Hepatocytes

Metaxalone	6β-Hydroxytestosterone formation			Specific Activity		
	Raw	Adjusted (μM)		(pmol/min/million cells)		Percent
(μM)	(μM)	Individual	Mean ± SD	Individual	Mean ± SD	of VC
40	0.05587[a]	<0.100	<0.101 ± 0.00238	<0.893	<0.905 ± 0.0213	101
	0.10413	0.104		0.930		
	0.08088[a]	<0.100		<0.893		

Abbreviations:
SD, standard deviation;
VC, vehicle control (1% Methanol);
[a]The observed analyzed value (μM) was below the lowest concentration on the standard curve (0.1 μM).
Note:
For all calculations above, the resulting values are shown with at least three significant figures for display purposes only.

Table 18 presents the results for CYP1A2. Under these experimental conditions, exposure to metaxalone at 40 μM induced CYP1A2 activity in human hepatocytes prepared from Donors 1, 2, and 3. For each of the three donors, the increases in CYP1A2 activity by metaxalone at 0.4 and 4 μM were not statistically significant ($p>0.05$; unpaired two-tailed t test).

Table 25 presents the results for CYP3A4. Metaxalone at the concentration of 40 μM induced CYP3A4 activity by about 21% in one of three donors tested, Donor 2. Therefore under these experimental conditions, exposure to metaxalone at 40 μM induced CYP3A4 activity in human hepatocytes prepared from Donor 2. The increase in CYP3A4 activity following treatment with metaxalone at 0.4 μM for Donor 2 was not statistically significant ($p>0.05$; unpaired two-tailed t test). CYP3A4 activity in the vehicle controls for Donor 1 and Donor 3 were below the lower limit of quantitation. Exposure of hepatocytes from Donors 1 and 3 to metaxalone at the concentrations tested did not induce CYP3A4 activity since the activity following treatment with metaxalone was still below the lower limit of quantitation at each tested concentration.

Table 21 presents the results for CYP2C9. Under these experimental conditions, exposure to metaxalone at 40 μM significantly reduced CYP2C9 activity in human hepatocytes prepared from Donors 1, 2, and 3. The observed changes in CYP2C9 activity following exposure to metaxalone at 0.4 and 4 μM were not statistically significant ($p>0.05$; two-tailed t test). Thus, under these experimental conditions, exposure to metaxalone at 40 μM inhibited CYP2C9 activity.

Table 23 presents the results for CYP2D6. CYP2D6 activity was below the lower limit of quantitation in the vehicle controls and for the metaxalone-exposed samples for Donor 1. However, under these experimental conditions, exposure to metaxalone at 40 μM significantly reduced CYP2D6 activity in human hepatocytes prepared from Donors 2 and 3. The observed changes in CYP2D6 activity following exposure to metaxalone at 0.4 and 4 μM were not statistically significant ($p>0.05$; two-tailed t test). Thus, under these experimental conditions, exposure to metaxalone at 40 μM inhibited CYP2D6 activity.

Any combination of the above-described elements in all possible variations thereof is encompassed by the invention unless otherwise indicated herein or otherwise clearly contradicted by context.

We claim:

1. A method of using metaxalone for treating a musculoskeletal condition, comprising

administering to a human patient metaxalone and an inhibitor or an inducer of CYP1A2;

informing the human patient that metaxalone is a substrate of CYP1A2 and that administration of metaxalone and an inhibitor or an inducer of CYP1A2 can affect plasma concentration, bioavailability, safety, efficacy, or a combination comprising at least one of the foregoing of metaxalone; and

monitoring the human patient's plasma concentration of metaxalone while metaxalone and the inhibitor or the inducer of CYP1A2 are administered to the human patient.

2. The method of claim **1**, additionally comprising

altering dosing of metaxalone based on the human patient's plasma concentration of metaxalone.

3. The method of claim **1**, wherein an inhibitor of CYP1A2 is administered to the human patient and the inhibitor of CYP1A2 is amiodarone, cimetidine, a fluoroquinolone, fluvoxamine, furafylline, interferon, methoxsalen, or mibefradil.

4. The method of claim **1**, wherein an inducer of CYP1A2 is administered to the human patient and the inducer of CYP1A2 is insulin, methyl cholanthrene, modafinil, nafcillin, beta-naphthoflavone, or omeprazole.

5. A method of using metaxalone for treating a musculoskeletal condition, comprising

administering to a human patient metaxalone and an inhibitor or an inducer of CYP2C19;

informing the human patient that metaxalone is a substrate of CYP2C19 and that administration of metaxalone and an inhibitor or an inducer of CYP2C19 can affect plasma concentration, bioavailability, safety, efficacy, or a combination comprising at least one of the foregoing of metaxalone; and

monitoring the human patient's plasma concentration of metaxalone while metaxalone and the inhibitor or the inducer of CYP2C19 are administered to the human patient.

6. The method of claim **5**, additionally comprising

altering dosing of metaxalone based on the human patient's plasma concentration of metaxalone.